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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,873	12/06/2004	Hilmar Meek Warenius	00030-003US1	1109

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EXAMINER	
HALVORSON, MARK	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
09/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,873	WARENIUS ET AL.	
	Examiner	Art Unit	
	Mark Halvorson	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-15 and 18-28* is/are pending in the application.

4a) Of the above claim(s) *6,9-15 and 18-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 5, 7 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 2, 5-15, 18-28 are pending.

Claim 6, 9-15 and 18-28 have been withdrawn.

Claims 1, 2, 5, 7 and 8 are under examination.

35 USC § 112 rejection withdrawn

The rejection of claims 1-5, 7 and 8 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of Applicants amendments to claim 1.

35 USC § 102(b) rejections withdrawn

The rejection of claims 1, 2 7 and 8 under 35 U.S.C. 102(b) as being anticipated by Hybridon (WO 99/27087, published June 3, 1999) is withdrawn in view of Applicants amendments to claim 1.

The rejection of claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (US Patent No: 6,004,939, issued Dec 21, 1999) is withdrawn in view of Applicants amendments to claim 1.

35 USC § 103 rejections maintained

The rejection of claims 1 and 5 under 35 U.S.C. 103(a) as being unpatentable over Hybridon (WO 99/27087, published June 3, 1999) as applied to claims 1, above, and further in view of Theryte Limited (WO 99/42821, publication date 26 August 1999) is maintained.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The claims are drawn to a method of screening for an agent effective in the treatment of a cancer, comprising selecting a putative agent that is likely to disrupt a function mediated by a critical normal gene product, which functions is required for a successful division and continued cell survival of cancer cells and which functions is not required for the successful division and continued cell survival of control cells; treating a cancer cell sample and a control cell sample with the putative agent, wherein the cancer cell sample consists of cancer cells in which the ratio of the levels of the CDK1 and CDK4 gene products is in the range of 0.6 to 1.6, and determining the cytotoxic effect and/or growth inhibiting effect of the putative agent on these samples; and identifying an effective agent which is more cytotoxic to, and determining the cytotoxic effect of, and/or the growth of the cancer cell sample than the control sample, Identifying an effective agent as an agent which is more cytotoxic to and/or more inhibiting to the growth of the cancer cell sample than the control cell sample, wherein the step of identifying an effective agent involves determination of the ratio of the levels of the CDK1 and CDK4 gene products in the cancer cell sample before and after treatment with the putative agent, wherein an effective agent is identified as an agent capable of altering the ratio in the levels of the CDK1 and CDK4 gene product in a cancer cell sample.

Hybridon discloses antisense molecules that bind to the CDK4 gene and inhibit the expression of CDK4 (page 15 line 1 to page 17 line 28) . Hybridon further discloses that other antisense molecules that inhibit CDK4 expression can be identified (page 17 line 30 to page 18 line3). The antisense molecules can be used for treating a mammal afflicted with a tumor associated with the aberrant expression of CDK4 (Abstract). An antisense molecule would suppress expression of the CDK protein and would disrupt all functions mediated by CDK4 including non-kinase and CKI sequestrating functions.

Hybridon does not disclose a cancer cell sample that consists of cells in which the CDK1 and CDK4 gene products are both elevated as compared with control cells in which the ratio of the levels of the CDK1 and CDK4 gene products is in the range of 0.6 to 1.6.

Theryte discloses that CDK1 and CDK4 proteins are elevated in cancer cells (Figs. 3 and 4) and that the ration of CDK4 to CDK1 is approximately 1 (Figs. 5 and 6).

One of ordinary skill in the art would have been motivated to apply Theryte's teaching of the diagnostic value of CDK1 and CDK4 levels in cancer to Hybridon's method of inhibiting CDK4 because Theryte states that the increased levels of CDK1 and CDK4 in cancers may be used in drug screening that might lead to more specifically toxic to cancer tissues (page 3, 3rd paragraph). Thus, it would have been prima facie obvious to combine Hybridon's method of inhibiting CDK4 with Theryte's finding of elevated levels of CDK4 and CDK1 in cancer.

Applicants argue that Theryte Ltd. actually teaches and suggests that there is a correlation between CDKI and CDK4 levels in P53 mutant human cancer cells Applicants argue that this description would not have led the skilled person to investigate the importance of these two gene products. Applicants argue that nowhere in Theryte is the skilled person taught that a cancer cell sample can be identified as one which consists of one or more cells in which the ratio of the levels of the CDKI and CDK4 gene products is in the range of 0.6 to 1.6. Applicants argue that there is nothing in the Theryte application that teach or suggest screening for an agent to treat cancer

by examining the ratio of CDKI to CDK4 when determining the effectiveness of a putative cancer treating agent.

Applicants' arguments have been considered but are not persuasive. The specification discloses that CDK4 acts to elevate CDK1, p9Ka and possibly CDK2, CDK6 and p27 by a mechanism that is independent of its role in the cell cycle. In response to Applicants arguments that the description in Theryte would not have led the skilled person to investigate the importance of these two gene products, Theryte discloses that disruption of the CDK1/CDK4 relationship in p53 mutant cells can be identified as a new target for anticancer therapy (page 3, 5th paragraph). In addition, Thryte discloses that because both the CDK1/CDK4 co-elevation and p53 mutations are confined to cancer cells and appear to be inter-related, they form in combination a complex target that is likely to prove the most specific one for cancer therapy that so far has been discovered. (Id).

In response to Applicants arguments that nowhere in Theryte is the skilled person taught that a cancer cell sample can be identified as one which consists of one or more cells in which the ratio of the levels of the CDKI and CDK4 gene products is in the range of 0.6 to 1.6, Theryte discloses that for cancer cells with mutated p53 the CDK1/CDK4 ratio is approximately 1.2 and for cancer cells with wild type p53 the CDK1/CDK4 ratio is between o.6 and 1.3. In response to Applicants arguments that there is nothing in the Theryte application that teach or suggest screening for an agent to treat cancer by examining the ratio of CDKI to CDK4 when determining the effectiveness of a putative cancer treating agent, Hybridon discloses the use of antisense molecules that bind to the CDK4 gene and inhibit the expression of CDK4 and would alter the ratio of CDK1 and CDK4 gene products. Hybridon discloses that the concentration of the CDK4 gene product was significantly decreased after the treatment with the CDK4 antisense molecule. (Fig. 4). It is noted that nowhere in the specification is it demonstrated that agents that are effective in the treatment of cancer alter the ratio of CDK1 and CDK4 gene products. Thus it is not clear if an effective agent increases or decreases the ratio of CDK1 and CDK4 gene products.

NEW REJECTIONS: based on amendments

Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 2, 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hybridon (WO 99/27087, published June 3, 1999) as applied to claims 1, above, and further in view of Theryte Limited (WO 99/42821, publication date 26 August 1999).

The claims are drawn to a method of screening for an agent effective in the treatment of a cancer, comprising selecting a putative agent that is likely to disrupt a function mediated by a critical normal gene product, which functions is required for a successful division and continued cell survival of cancer cells and which functions is not required for the successful division and continued cell survival of control cells; treating a cancer cell sample and a control cell sample with the putative agent, wherein the cancer cell sample consists of cancer cells in which the ratio of the levels of the CDK1 and CDK4 gene products is in the range of 0.6 to 1.6, and determining the cytotoxic effect and/or growth inhibiting effect of the putative agent on these samples; and identifying an effective agent which is more cytotoxic to, and determining the cytotoxic effect of, and/or the growth of the cancer cell sample than the control sample, Identifying an effective agent as an agent which is more cytotoxic to and/or more inhibiting to the growth of the cancer cell sample than the control cell sample, wherein the step of identifying an effective agent involves determination of the ratio of the levels of the CDK1 and CDK4 gene products in the cancer cell sample before and after treatment with the putative

agent, wherein an effective agent is identified as an agent capable of altering the ratio in the levels of the CDK1 and CDK4 gene product in a cancer cell sample, wherein the critical normal gene product is human CDK4, wherein the region of human CDK4 gene product mediating the function required for successful division and controlled cell survival is a region between amino acids 172-285. The actual function of CDK4 being screened for is not defined in the claims.

Hybridon discloses antisense molecules that bind to the CDK4 gene and inhibit the expression of CDK4 (page 15 line 1 to page 17 line 28) . Hybridon further discloses that other antisense molecules that inhibit CDK4 expression can be identified (page 17 line 30 to page 18 line3). The antisense molecules can be used for treating a mammal afflicted with a tumor associated with the aberrant expression of CDK4 (Abstract). An antisense molecule would suppress expression of the CDK protein and would disrupt all functions mediated by CDK4 including non-kinase and CKI sequestrating functions. Thus, the antisense molecule would disrupt the undisclosed function of CDK4 mediated by a region of CDK4 between amino acids 172-285.

Hybridon does not disclose a cancer cell sample that consists of cells in which the CDK1 and CDK4 gene products are both elevated as compared with control cells in which the ratio of the levels of the CDK1 and CDK4 gene products is in the range of 0.6 to 1.6.

Theryte discloses that CDK1 and CDK4 proteins are elevated in cancer cells (Figs. 3 and 4) and that the ration of CDK4 to CDK1 is approximately 1 (Figs. 5 and 6).

One of ordinary skill in the art would have been motivated to apply Theryte's teaching of the diagnostic value of CDK1 and CDK4 levels in cancer to Hybridon's method of inhibiting CDK4 because Theryte states that the increased levels of CDK1 and CDK4 in cancers may be used in drug screening that might lead to more specifically toxic to cancer tissues (page 3, 3rd paragraph). Thus, it would have been prima facie obvious to combine Hybridon's method of inhibiting CDK4 with Theryte's finding of elevated levels of CDK4 and CDK1 in cancer.

Summary

Claims 1-5, 7 and 8 stand rejected

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Halvorson, PhD whose telephone number is (571) 272-6539. The examiner can normally be reached on Monday through Friday from 8:30am to 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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571-272-6539

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